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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/882,415 06/25/97 ZHANG

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EXAMINER

GARCIA, M

ART UNIT	PAPER NUMBER
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1627

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DATE MAILED:

02/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	08/882,415	Applicant(s)	Zhang et al
Examiner	Maurie E. Garcia, Ph. D.	Group Art Unit	1627

Responsive to communication(s) filed on Nov 13, 2000

This action is FINAL.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle 1035 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire THREE month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

Claim(s) 1-16 and 18-21 is/are pending in the application.

Of the above, claim(s) 20 and 21 is/are withdrawn from consideration.

Claim(s) 19 is/are allowed.

Claim(s) 1-4, 6, 8-12, 16, and 18 is/are rejected.

Claim(s) 5, 7, and 13-15 is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's Response filed November 13, 2000 is acknowledged. The Declaration under 37 CFR 1.132 is also acknowledged. Claims 1, 8, 12, 16 and 18-19 were amended and claim 17 was cancelled. Therefore, claims 1-16 and 18-21 are pending.
2. This application contains claims 20 and 21 drawn to an invention nonelected with traverse in Paper No. 8. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Rejections/Objections

3. All previous rejections under 35 USC 112, second paragraph and 35 USC 102 and 102/103 are withdrawn in view of the arguments and amendments. The rejections under 35 USC 103 over Duschl et al or Lopez et al in view of Kumar et al; and over Duschl et al in view of Wang et al are also withdrawn in view of the arguments and amendments.
4. Applicant's arguments and the declaration under 37 CFR 1.132 by Zhang filed November 13, 2000 have been fully considered and are sufficient to overcome the rejection of claim 19 under 35 USC 112, first paragraph. Also, the objections to claims 1, 16, 18 and 19 are withdrawn in view of applicant's amendments thereto.

Maintained Rejections
Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-3, 6 and 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singhvi et al (Reference AY on Applicant's PTO-1449) in view of Duschl et al.

Singhvi et al teach a method of patterning SAMs that is identical to that of the instant invention (microcontact printing), making "defined features" with "specific patterns" for placing cells in "predetermined locations and arrays" (see Abstract). The method is shown in Figure 1 of the reference and produces a solid

support that has a patterned monolayer thereon. The pattern comprises regions that are adhesive to proteins and nonadhesive to proteins due to the stamping of hexadecanethiol (adhesive) and then filling in of the non-printed regions with PEG-terminated alkanethiol (nonadhesive) (see page 696). The solid support is exposed to a protein after printing.

Singhvi et al lacks the teaching of forming a peptide monolayer directly by depositing a peptide in the non-printed regions. However, Duschl et al teach patterned peptides directly bound to a gold substrate by the interaction of the thiol sidechain with the surface. The peptides have the structure CY(NANP)₃ – with C being the terminal reactive group (terminal amino acid), Y the central linker and (NANP)₃ the presenting group (see pages 1230-1231), as shown in Figure 1B and Figure 3. The peptides of Duschl et al are deposited into predefined regions (see Figure 1).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to make the patterned monolayers of Singhvi et al using directly bound peptides to form monolayers in the non-printed regions. One would have been motivated to do so in order to have the advantages of a patterned monolayer structure as taught by Duschl et al (see Discussion, page 1236) utilizing the ease of the stamping techniques as taught by Singhvi et al (see page 698).

Response to Arguments

8. Applicant's arguments filed November 13, 2000 have been fully considered but are not found persuasive. The examiner's rationale is set forth below.

9. Applicant argues each of the references separately (see Response, pages 19-20). In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The examiner maintains that the *combined* teachings of the references render the claimed invention *prima facie* obvious (see paragraphs 10-11 below).

10. Applicant also argues that there is no motivation to combine (Response, page 19, bottom through page 20, top) stating that "Duschl does not provide the motivation..." and "Duschl does not suggest any benefit...". In response to this argument, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

11. However, the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected

beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). In the instant case, the beneficial result that would be produced by the *combination* of the references is the creation of a patterned monolayer of peptides that allow the “ differential binding of proteins” (see page 1233, 2nd column of Duschl) with the ease of the stamping techniques as taught by Singhvi et al (see page 698).

12. Lastly, applicant argues that there would be not be a reasonable expectation of success due to the “unpredictability of replacing the alkanethiol in the compositions of Singhvi with a peptide” (Response, page 20). Applicant also argues that the examiner’s previous rejection under 35 USC 112, first paragraph is evidence in support of this position. The examiner respectfully disagrees. The rejection at hand is directed at the embodiment of the instant invention that requires first printing with a compound in the relief of the desired pattern and then depositing peptides in the unmodified regions of the pattern. The previous rejection under 35 USC 112 was directed at the embodiment of direct printing peptides using a stamp (i.e. no first printing with a compound in the relief of the desired pattern).

13. Therefore, the examiner maintains that there would be a reasonable expectation of success for the following reasons. The rejection above states that Singhvi et al teach a patterned SAM containing regions that are adhesive to proteins and nonadhesive to proteins due to the stamping of hexadecanethiol (adhesive) and then filling in of the non-

printed regions with PEG-terminated alkanethiol (nonadhesive) (see page 696). The solid support is exposed to a protein after printing. The examiner recognizes that Singhvi et al lacks the teaching of forming a peptide monolayer *directly* by depositing a peptide in the non-printed regions. However, Duschl et al teach patterned peptides directly bound to a gold substrate by the interaction of the thiol sidechain with the surface. Thus what the examiner is interpreting to have a reasonable expectation of success to one of ordinary skill is to substitute the thiol containing peptides of Dushl for the PEG-terminated alkanethiol of Singhvi. Thus, the combination of references renders obvious the claimed monolayers of directly bound peptides formed in the non-printed regions.

New Rejections - Necessitated by Amendment
Claim Rejections - 35 USC § 103

14. Claims 1-4, 6, 8-12, 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duschl et al (of record) in view of Kumar et al (US 5,512,131, of record) and Singhvi et al (of record).

Duschl et al teach “the fabrication of patterns with contrasting surface properties on gold substrates” (see Abstract). Self-assembled monolayers (SAMs) of peptides are formed in a pattern having ordered areas where the peptides are and are not bound, as shown in Figure 1B and Figure 3. The patterns are determined by the properties of the mixture of palmitic acid and sulfur-bearing lipid (page 1229, 2nd column). The “patterned surface for the differential binding of proteins” (see page 1233, 2nd column) is formed by linear peptides containing a terminal cysteine group, which reads directly on claims 8-11. The peptides are

directly bound to a gold substrate by the interaction of the thiol sidechain with the surface. The peptides have the structure CY(NANP)₃ – with C being the terminal reactive group (terminal amino acid), Y the central linker and (NANP)₃ the presenting group (see pages 1230-1231). Although the peptides of Duschl have only a 1 amino acid linker, it would be *prima facie* obvious to modify the peptides of Duschl et al to have a longer linking group. One of ordinary skill in the art would realize that it is the NANP sequence that possesses the affinity for the target and the length of linker could be modified to modulate monolayer formation or properties.

Duschl et al lack the teaching of the newly added limitation of the “printed pattern” and making the SAMs directly on glass substrates. However, such “printed pattern” SAMs were known in the art at the time of filing. For example, Kumar et al teach a method of patterning SAMs (microcontact printing) that is identical to that of the instant invention and teach that “a wide variety of materials and SAM-forming molecular species are suitable” (see column 10, lines 40-45 and 57-64). Kumar et al teach that “portions of the material surface that are not coated with a stamped SAM pattern may be filled in with another SAM forming species” (see Abstract and Figure 1a).

Additionally, Singhvi et al teach a method of making a “printed pattern” SAM that is also identical to that of the instant invention (microcontact printing), making “defined features” with “specific patterns” for placing cells in “predetermined locations and arrays” (see Abstract). The method is shown in

Figure 1 of the reference and produces a solid support that has a patterned monolayer thereon. The pattern comprises regions that are adhesive to proteins and nonadhesive to proteins due to the stamping of hexadecanethiol (adhesive) and then filling in of the non-printed regions with PEG-terminated alkanethiol (nonadhesive) (see page 696). The solid support is exposed to a protein after printing. Singhvi et al lacks the teaching of forming a peptide monolayer directly by depositing a peptide in the non-printed regions.

It was also well known in the art at the time of filing that such monolayers could be made directly on glass with the appropriate choice of reactive groups. Kumar et al list silica and glass as some of the preferred materials (see column 10, lines 40-45 and 57-64).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to use the thiol containing peptides of Dushl to form a “printed pattern” SAM as taught by Kumar et al and Singhvi et al. One of ordinary skill in the art would have been motivated to use the peptides of Duschl to obtain “differential binding of proteins” (see page 1233, 2nd column of Duschl) and would have a reasonable expectation of success since the peptides of Duschl are taught to be capable for forming SAMs and have the requisite thiol groups.

One would also have been motivated to use glass as a substrate for the SAM in order to have a transparent substrate material for ease in analysis of the patterned SAMs (and binding partners thereof) as also taught by Kumar et al (column 15 line 66-column 16 line 4).

Status of Claims/Conclusion

15. Claim 19 is allowable over the prior art. Also, claims 5, 7 and 13-15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie E. Garcia, Ph.D. whose telephone number is (703) 308-0065. The examiner can normally be reached on Monday-Thursday from 8:30 to 6:00 and on alternate Fridays.

18. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



DR. JYOTHSNA VENKAT PH.D
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Maurie E. Garcia, Ph.D.
February 11, 2001